Eur Arch Otorhinolaryngol (2013) 270:1729–1735
DOI 10.1007/s00405-012-2213-2

HEAD AND NECK

Pre-operative tracheostomy does not impact on stomal recurrence and overall survival in patients undergoing primary laryngectomy

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Received: 18 June 2012 / Accepted: 26 September 2012 / Published online: 9 October 2012

Abstract Pre-operative tracheostomy (POT) to secure a critical airway up to several weeks before definitive laryngectomy in patients with laryngeal cancer has been proposed as a risk factor for poor oncologic outcome. Few modern papers, however, examine this question. The aim of this study is therefore to determine whether POT affects oncologic outcome with an emphasis on stomal/peristomal recurrence. This is a retrospective case note review of 60 consecutive patients undergoing curative primary total laryngectomy (TL) for advanced laryngeal squamous cell carcinoma (SCC). Demographic, staging, treatment and outcome data were collected. 27/60 (45 %) patients had POT and 33/60 did not. No patient underwent laser debulking. Median age was 62 years (39–90 years) and median follow-up of survivors was 31 months. 5-year overall survival (OS), disease-specific survival (DSS) and local recurrence-free survival (LRFS) of patients undergoing POT versus no POT was 28 versus 39 % ($p = 0.947$), 55 versus 46 % ($p = 0.201$) and 96 versus 88 % ($p = 0.324$) respectively. No statistically significant difference in OS, DSS and LRFS was found between patients undergoing POT and those not. Despite the relatively small case series, this evidence should reassure surgeons without the ability to perform trans-oral debulking that they should not hesitate to perform tracheostomy on a patient with airway obstruction due to laryngeal cancer. Appropriate definitive treatment meant that POT was not a risk factor for poor oncological outcome in our series.

Keywords Laryngectomy · Tracheostomy · Squamous cell carcinoma · Local recurrence · Airway

Introduction

Even in the present day, the initial presentation of a patient with advanced laryngeal cancer can be imminent airway obstruction. Three options exist to relieve this problem: trans-oral debulking (TOL) often with a laser, tracheostomy and emergency laryngectomy. The latter technique has largely been abandoned [1] and there has been a move away from pre-operative tracheostomy (POT) towards TOL in recent years. This move has been driven by studies which showed that POT was associated with a higher risk of stomal/peristomal recurrence [2–5], and that TOL could reliably secure the airway [6].

However, on occasion, POT is the easiest way of securing a critical airway. Indeed, TOL can be limited in its application as it requires specialist equipment and experience, in both surgical and anaesthetic fields. TOL also has the potential disadvantage of post-operative oedema [7] and rapid tumour re-growth necessitating repeat debulking.

Many studies investigating the oncological risk of POT are now quite old. Furthermore, the treatment paradigms and modalities for laryngeal cancer have changed significantly in the last 20 years and it is not clear whether the previous studies on POT are still applicable.

This study was previously presented at the British Association of Head and Neck Oncology meeting, April 28th 2011. Royal Society of Medicine, Laryngology section meeting, February 4th 2011.

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Our unit regularly receives patients who have presented with airway compromise to surrounding smaller hospitals where they have undergone emergency tracheostomy before being transferred to us for definitive management. Indeed our unit still prefers POT to TOL and the aim of this study was therefore to analyse the impact of POT on oncological outcome in a contemporary patient cohort undergoing primary TL.

Materials and methods

After local ethics and audit committee approval, a retrospective case note review was performed of 60 consecutive patients who underwent primary TL for locally advanced laryngeal squamous cell carcinoma (SCC) performed with curative intent between 2003 and 2010. Patients who underwent primary chemoradiotherapy, partial laryngectomy or those treated palliatively from the outset were therefore excluded.

Patients' demographic, staging, pre-operative imaging, treatment and outcome data were collected using case notes, surgeons' logbooks and electronic patient records (EPR). Patient factors analysed included age at procedure and gender which were retrieved from the hospital electronic database. Primary site, cTNM classification, type of procedure, extent of neck dissection (ND) and pre-operative tracheostomy (POT) were retrieved from operative records and radiological imaging reports. Histological features such as degree of differentiation, the presence of extra-capsular spread, sarcolemmal/perineural/perivascular invasion, the presence of a cohesive front, thyroid gland involvement and adequacy of the pathological margin of excision were collected from surgical histopathological results.

All patients underwent pre-operative computerized tomography (CT) scanning of the neck and thorax, magnetic resonance (MR) scanning when indicated and had their treatment planned in our multidisciplinary head and neck tumour (MDT) board meeting. All patients were staged M0 and treated with curative intent. Both version 6 and 7 of the AJCC staging manual [8, 9] were used as the study period straddled the change in 2009.

At the time of POT, the approach outlined in Table 1 was systematically adopted whenever possible.

All patients underwent primary TL in our unit, including comprehensive central compartment (level VI) neck dissection [10] with lateral neck dissections as agreed by the MDT board meeting. All patients with POT had the tracheal window excised and sent for histological analysis. At the time of definitive surgery, frozen sections were used to confirm satisfactory margins with critical analysis of the lower tracheal margins following excision of the POT tract as part of an en bloc surgical specimen. All patients had

Table 1 Modern approach to total laryngectomy

At the time of POT
Excision and histological analysis of the excised tracheal window and the thyroid isthmus and Delphian node at POT
Placement of the tracheostomy between the 2nd and 4th tracheal rings
Inspection of the lower margin of the trachea before tube placement
At the time of definitive TL
Minimal interval time between POT and TL
Comprehensive wide field TL with lateral compartment neck dissections
Excision of the tracheostomy tract at definitive surgery
Critical appraisal of thyroid involvement, including evaluation of the invasion of the thyroid gland, ipsilateral hemithyroidectomy with isthmusectomy on the side of the tumour or total thyroidectomy when indicated
Frozen section margin control especially of the lower tracheal margin
Central compartment (level VI) neck dissection
Post-operative management
Post-operative radiotherapy or chemo-radiation therapy

critical evaluation and management of the thyroid gland. This included ipsilateral thyroid lobectomy with isthmusectomy on the side of the tumour or total thyroidectomy when pre-operative staging suggested thyroid involvement, an approach validated by earlier research [11]. The treatment plan included post-operative radiotherapy (PORT) for all patients and after 2008, patients with positive margins or extra-capsular spread were planned for post-operative chemoradiotherapy (CRT). For a variety of reasons, not all patients were able to complete adjuvant treatment.

Local recurrence (LR) was defined as recurrent squamous cell carcinoma (SCC), diagnosed within 5 years of initial treatment involving the immediate stomal and peri-stomal region. Regional recurrence (RR) was defined as recurrent SCC involving the cervical nodes level 1–5. Distant recurrence was diagnosed either clinically or on imaging studies including ultrasound guided fine needle aspiration, CT or positron emission tomography (PET) scanning. All recurrences were biopsy proven except in those patients in which it was felt that either co-morbid status or disease progression meant that invasive biopsies were not indicated. All cases were discussed within the MDT, and those patients not fit for biopsy were considered as recurrence by consensus based on clinical or imaging examination.

Evidence of patients' death was taken from hospital records and death certificates where available. All patients with active disease at last follow-up who died of unknown causes were considered as having died of disease.

Statistical analysis of overall survival (OS), disease-specific survival (DSS) and local recurrence-free survival

Table 2 Description of patients and disease

Factor	Number of patients (%)
Ablative	
Total laryngectomy	31 (52 %)
Plus Pharyngectomy	29 (48 %)
Location	
Subglottic	1 (2 %)
Glottic	4 (7 %)
Supraglottic	22 (37 %)
Transglottic	20 (33 %)
Hypopharynx	12 (20 %)
Incomplete records	1 (2 %)
pT stage	
T3	15 (25 %)
T4	44 (73 %)
Incomplete records	1 (2 %)
pN stage	
N0	18 (30 %)
N1	10 (17 %)
N2a	1 (2 %)
N2b	13 (22 %)
N2c	14 (23 %)
N3	1 (2 %)
Incomplete records	3 (5 %)
Histological differentiation	
Well differentiated	3 (5 %)
Moderately differentiated	25 (42 %)
Poorly differentiated	29 (48 %)
Incomplete records	3 (5 %)
Extranodal spread in N+	($n = 39$)
Yes	27 (69 %)
No	11 (28 %)
Incomplete records	1 (3 %)
Tracheostomy	
POT	27 (45 %)
No POT	33 (55 %)

(LRFS) were calculated using the Kaplan–Meier method. The log-rank test was used for univariate, and cox-regression model for multivariate analysis (SPSS, Chicago, Illinois, v19). Comparison of subgroups was performed using the Fishers exact test.

Results

Sixty patients with median age of 62 years (39–90 years) were analysed. Forty-nine were male (82 %), 11 were female (18 %). The median follow-up was 16 months (range 1–91 months), with a median follow-up for survivors of 31 months (range 4–91 months). 27/60 (45 %) patients had POT. No patients had TOL. The majority of patients undergoing POT had awake fibreoptic intubation in line with anaesthetic guidelines [12].

Procedure, location of primary, pT and pN stage and histology are shown in Table 2. All patients underwent TL and 29 also had partial pharyngectomy (48 %). Forty-eight had laryngeal (80 %) and 12 hypopharyngeal primaries (20 %). All patients had comprehensive central neck dissection. Fifty-five patients underwent bilateral (92 %) lateral neck dissection and five patients had unilateral (8 %) neck dissection.

Two patients died within 30 days of surgery (perioperative deaths) due to carotid blow out. Both had extensive disease peeled off the carotid during surgery and had involved margins. A further 34 patients died during follow-up, 24 of these from their disease (5 LR, 2 RR and 17 DR).

For the whole cohort of patients, 5-year overall survival (OS), disease-specific survival (DSS) and local recurrence-free survival (LRFS) were 36, 51, 92 % respectively (Fig. 1).

As expected, the presence of nodal metastasis predicted worse disease-specific survival (pN0 5y DSS 74 vs pN + 32 %, $p = 0.008$). This was, however, most likely because $N =$ stage is a predictor of distant metastasis. Indeed loco-regional control rates were excellent. No significant association was found between tumour site and risk of recurrence, though this was probably due to small numbers.

POT versus no POT

1/27 (3.7 %) patients with POT had local recurrence during follow-up compared to 4/33 (12 %) patients without POT. 5-year overall survival (OS), disease-specific survival (DSS) and local recurrence-free survival (LRFS) of patients undergoing POT versus no POT was 28 versus 39 % ($p = 0.947$), 55 versus 46 % ($p = 0.201$) and 96 versus 88 % ($p = 0.324$), respectively.

POT was therefore not statistically associated with poorer outcome in terms of OS, DSS or LRFS (Figs. 2, 3, 4).

Subgroup analysis/bias

Due to the non-randomised nature of our study, we analysed whether the POT and non-POT group were similar in terms of ages, co-morbidities and TNM classification. The groups were similar though the POT group had a higher rate of pT3 than pT4 disease (Table 3). This counter-intuitive result did not show any significant correlation

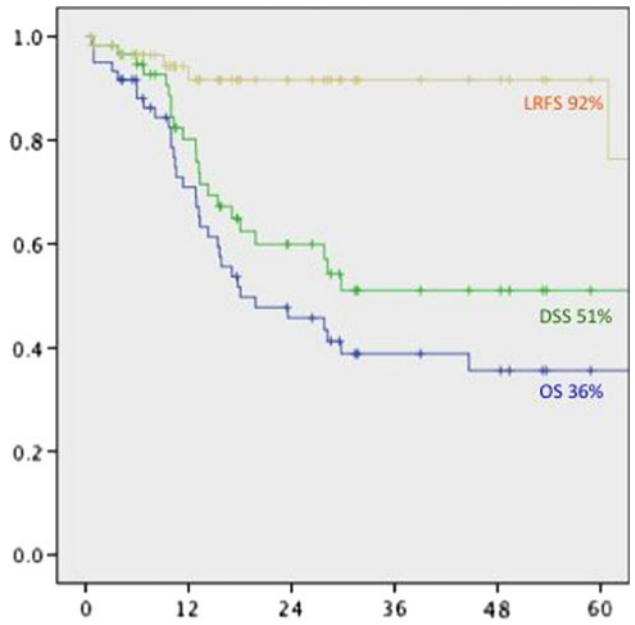

Fig. 1 Kaplan–Meier survival for the whole cohort

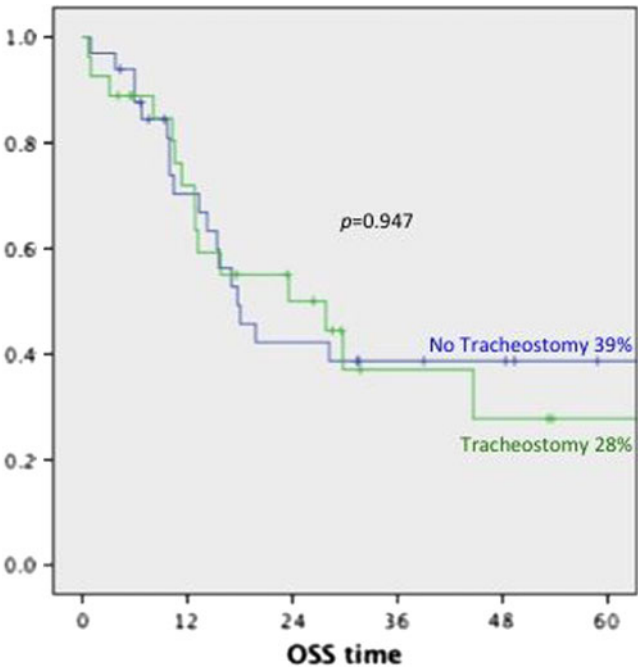

Fig. 2 Overall survival stratified by POT

with likelihood of POT (data not shown). Further subgroup analysis was performed by pT classification. Again POT was not predictive of outcome in either subgroup when analysed separately. POT remained a non-significant prognostic factor in outcome analysis of the T-classification subgroups i.e. pT3 POT versus pT3 non-POT and pT4 POT versus pT4 non-POT.

We further reanalysed our data assuming the incomplete records were either "positive" or "negative". In no instance did this change our result that there was no statistically significant association between POT and outcome.

Overall, we feel the patients who underwent POT were globally more compromised by their disease and co-morbidities and therefore would have expected these patients to perform worse than patients who did not undergo POT. The fact that we did not find a significant difference is therefore all the more striking.

Discussion

Laryngeal cancer is the only cancer for which survival rates have worsened over the last 20 years [13, 14]. The reasons for this have been contested [14–16] and potentially include worsening co-morbidities and the increased use of chemoradiation. Surgically speaking we can only focus on local and regional control and this paper addresses an important question regarding the risk of stomal/local recurrence.

Stomal recurrence following primary total laryngectomy (TL) for squamous cell carcinoma occurs in 2–15 % [17, 18] and has been defined as "a diffuse infiltration of neoplastic tissue at the junction of the trachea and skin" [17]. It is difficult to distinguish from spread from local level VI lymph nodes and the thyroid gland. Indeed in this paper we have not attempted to distinguish between these particular types and classify all stomal/peri-stomal recurrences as LR. Patients presenting with local recurrence have a dismal outcome with approximately 50 % presenting in the first year after completion of treatment [3, 4] and 80 % dying in the first 2 years after completion of treatment [19].

Pre-operative tracheostomy (POT) performed up to several weeks before definitive laryngectomy is one of several risk factors identified originally in the 1960s as being associated with increased risk of LR (Table 4). Since that time several papers have shown a poor outcome with POT [3, 5, 20] and others have found no relation [21–26].

Intuitively it seems plausible that POT might disrupt the primary tumour, seed the tract and therefore lead to worse local control (Fig. 5). Some authors have argued to place the tracheostomy low [27] in order to avoid any subglottic extension of the tumour, whereas others have argued for a high tracheostomy [17] which can then be more easily completely excised at the time of definitive laryngectomy. Theoretically also any time delay between the POT and the definitive TL would allow the seeded cancer to more effectively establish itself in the fresh tracheostomy wound bed.

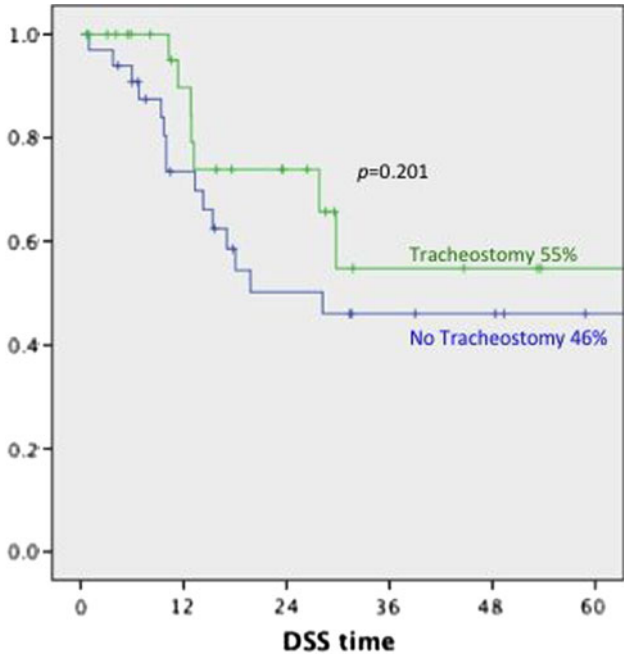

Fig. 3 Disease-specific survival stratified by POT

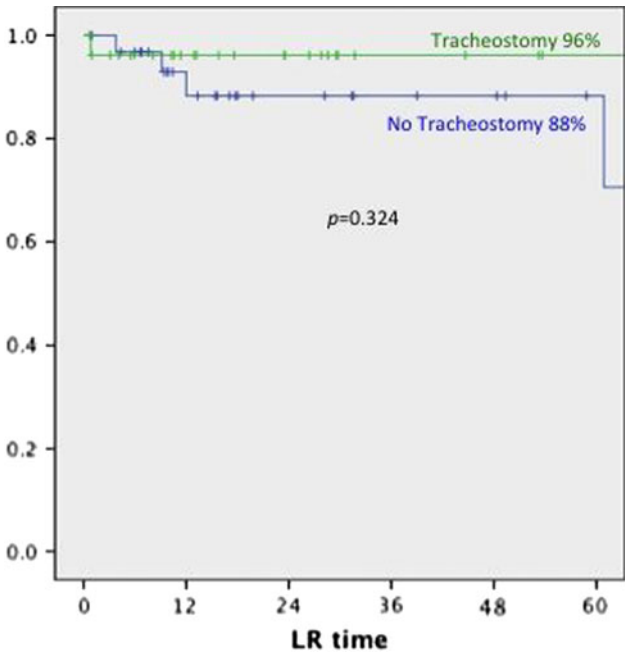

Fig. 4 Local recurrence-free survival stratified by POT

Evidence for the intuitive risk of POT comes from diverse sources. For example, there are case reports describing stomal recurrence in the setting of non-laryngeal/hypopharyngeal primaries. This raises the suspicion that cancer cells are able to inoculate the fresh tracheostomy wound [28, 29]. Stell [4] reported one case of a patient who had a maxillectomy performed with a covering tracheostomy who developed recurrence around the tracheostomy site 2 years later. McGurk [30] also reports three cases of patients who had a prophylactic tracheostomy for intra-oral resections that developed recurrence at the tracheostomy site. Clayman et al. [31] reported two cases of stomal recurrence with oropharyngeal primaries. There are even case reports of gastric metastasis from oral squamous cell carcinoma following PEG insertion [32]. Supporting these case reports are laboratory studies which have investigated vital looking tumour cells recovered from tracheal swabs or endo-tracheal tubes [33]. Though these could not be grown on intact mucosa, suspicions remain about them seeding a fresh tracheostomy wound.

Overall, however, we do not have a particularly good understanding of how LR occurs [19]. The terminology used in the literature is not necessarily consistent making meta-analyses difficult. Some authors use the word "recurrence" when actually describing residual disease following incomplete excision or when potentially positive central compartment lymph nodes have not been addressed as part of the definitive treatment. Other papers use the term stomal recurrence and it is not clear if this would include direct spread from level VI or the thyroid. Others do not differentiate between primary and salvage laryngectomy.

Furthermore, much of the literature quoted is quite old. Nowadays, with the increasing use of chemoradiotherapy, primary laryngectomy is often reserved for patients with

Table 3 Comparison of POT and non-POT groups

	Number of patients undergoing POT $N = 27$	Number of patients without POT $N = 33$	p value (Fischer's exact test)
Gender			
Male	23	26	0.53
Female	4	7	
Age (years)			
<60	10	16	0.80
>60	17	17	
pT stage			
T3	10	5	0.03
T4	17	27	
N0/N+			
N0	9	9	1.00
N+	17	22	
Stage			
Stage III	4	3	0.17
Stage IV	23	30	

Table 4 Risk factors thought to be associated with poor outcome following total laryngectomy

Risk factors [4]
Size of tumour
Location of tumour (e.g. subglottic)
Lymph node involvement (e.g. paratracheal)
Incomplete removal of tumour
Inoculation of tumour cells
Pre-operative tracheostomy
Endotracheal intubation

the most advanced local disease meaning that it is not necessarily possible to compare old data with modern series. The exact description of TL is also missing from many papers (for example whether the central compartment or thyroid was removed) again making comparisons difficult. We therefore felt that a consistent modern surgical approach in a modern patient cohort was needed to look at whether POT affects outcome following primary TL.

This is an important question, as even in the twenty-first century, many patients with advanced laryngeal cancer present with such severe airway compromise as to require emergency airway management. Though several protocols exist as to how to judge how severely compromised an airway is [12, 34], often objective measures of respiratory rate, fatigue, pulse oximetry etc. interplay with subjective measures of stridor and feelings of panic from both the patient and surgeon.

Securing a safe airway allows for appropriate investigations and staging as well as allowing fully informed consent before definitive treatment. Although laser surgery has theoretical oncological advantages, as it prevents disruption to tissue planes and minimises the chance of tumour seeding, it intuitively is not quite as safe as a POT in terms of securing the airway as there remains the potential risk of post-operative oedema [7], aspiration, and tumour re-growth. Furthermore, both the surgical and anaesthetic skills and instruments required to perform such procedures are often not available out of office hours or in smaller hospitals where such patients may present. Even if patients can be temporarily stabilised with inhalational therapies, some more advanced lesions are just not amenable to TOL. In such patients, POT may be the only safe option for the airway, irrespective of oncological concerns.

It must be stated, however, that our study is not a comparison of TOL versus POT, but rather a reassurance to surgeons who can be faced with a critical airway and no access to more advanced airway techniques. Our contention is that with sufficiently aggressive definitive management as described in Table 1, carried out within a reasonably short timeframe from the POT, that any increased risk associated with POT can be eliminated.

We would also like to highlight the multi-modal nature of our treatment which uses adjuvant post-operative irradiation of the surgical bed and bilateral neck nodes to reduce the risk of loco-regional recurrence [35]. To further improve locoregional recurrence rates [36, 37], post-operative chemoradiation [38] with high dose cisplatin and 60–66 Gy in 30–33 daily fractions has become the standard of care in our unit since 2008 for patients with positive margins and/or extracapsular spread [39], the two most unfavourable parameters.

In conclusion, management of the compromised airway in advanced laryngeal carcinoma remains a challenge. Whilst it is important that teams dealing with head and neck cancers are familiar with the use of TOL and endolaryngeal surgical techniques, our results are in keeping

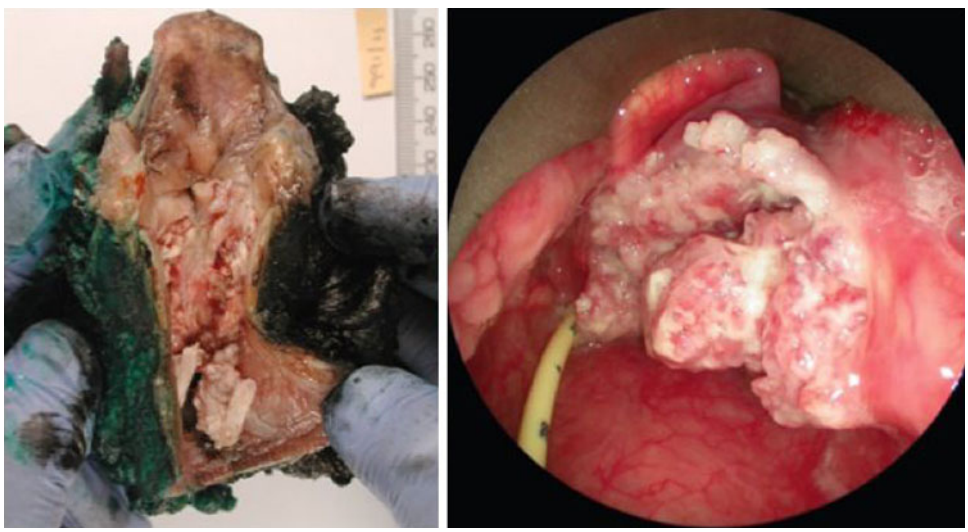

Fig. 5 Involvement of POT site in cancer

with more recent studies, which suggest that POT is not necessarily related to poor oncological outcome. It is a technique that can be easily taught, requires standard equipment available in all operating theatres and is suited to almost all advanced laryngeal lesions. Despite limitations imposed by the cohort size and potential lack of power, this paper provides evidence that POT is not a risk factor for poor outcome.

Conflict of interest None.

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